The Lymphocyte and Multiple Sclerosis

MANY INVESTIGATORS consider an exogenous agent as the primary etiologic factor in the development of multiple sclerosis (MS). However, delayed hypersensitivity involving antigens of the central nervous system is the hypothesized pathogenetic mechanism responsible for the clinical expression of the disorder.

Two aspects related to delayed hypersensitivity have been demonstrated in multiple sclerosis which support this model of pathogenesis, namely (1) evidence of host sensitization to encephalitogenic protein which may result in lymphocytes capable of damaging myelin and (2) a lymphotoxic factor which may represent a bodily defense from self-destruction.

In vitro techniques for the detection of delayed hypersensitivity are well established. Upon exposure to specific antigens, a sensitized population of lymphocytes will undergo morphological transformation into lymphoblast-like cells with associated increases in deoxyribonucleic acid (DNA), ribonucleic acid (RNA) and protein synthesis. The release of several functionally distinct lymphocyte products, such as macrophage migration inhibition factor (MIF), appears to be the culmination of this complex biochemical process.

In the presence of encephalitogenic protein, the putative antigen of multiple sclerosis, peripheral blood lymphocytes of MS patients experience these same morphological and biochemical alterations. It has also been demonstrated that such lymphocyte stimulation results in the elaboration of MIF. These experiments do help substantiate the theory of autoimmunity in MS, as did the earlier study by Berg and Källen. Their work established that lymphocytes from ME patients during exacerbation could exert a toxic effect on neurologia in tissue culture. However, it must be noted that disparate results have been reported concerning the morphological and metabolic changes of MS lymphocytes stimulated by encephalitogenic protein.

The complex association of the lymphocyte and MS is further obscured by the recent description of a transiently appearing serum protein which is specifically toxic to lymphocytes. The toxic effect of this heat-stable, small molecular weight protein is exerted through inhibition of DNA-directed RNA synthesis within the lymphocyte. The presence of this lymphotoxic factor is most commonly detected during exacerbation of multiple sclerosis. Therefore, it has been suggested that this factor may be the result of a host-defense relation against self-destruction.

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REFERENCES

Stjernholm RL, Wheelock EF, van den Noort S: A lymphotoxic factor in multiple sclerosis serum. J Reticuloendothel Soc 8:334-341, Oct 1970

Bartfeld H, Atoynatan T: Lymphocyte transformation in multiple sclerosis. Brit Med J 2:91-92, Apr 11, 1970

Berg O, Källen B: Effect of mononuclear blood cells from multiple sclerosis patients on neuroglia in tissue culture. J Neuropath Exp Neurol 23:550-559, Jul 1964

Cerebral Death Criteria

CONCEPTS AND DEFINITIONS of death have come under increasing discussion in recent years. This has largely resulted from improved resuscitation techniques and the development of life support systems which may at times leave patients with devastating brain damage, some in irreversible coma. Although in a state of "cerebral death," they may not meet the traditional criteria of "systemic death," such as irrevocable absence of heartbeat. The ability to preserve the patient in this mechanically maintained state poses frequent problems in the widespread use of organ transplants. It also presents the physician and family with a dilemma having ethical, moral, legal and financial repercussions. These matters are as yet unresolved.

The most widely held definition of irreversible coma appeared in 1968 and has become known as the "Harvard Criteria." There have been some subsequent refinements to the original definition which still basically is as follows: (1) Unreceptivity and unresponsivity to external (verbal and painful) stimuli; (2) No spontaneous movement or spontaneous respirations; (3) Absence of reflexes (deep tendon, plantar, corneal, pharyngeal reflexes), fixed dilated pupils, absence of eye movements even with ice water irrigation of the ear canals; and (4) A flat electroencephalograph (a linear or isoelectric electroencephalogram tracing) which is of great confirmatory value. Technical standards were described in order that the test be properly performed.

These features were to be rechecked 24 hours later and were not to have changed in that period. The validity of the diagnosis of irreversible cerebral dysfunction was dependent on the exclusion